

Application No.: 10/076,071

**Amendments to the Claims:**

This listing of claims will replace all prior versions and listings of claims in the application.

**Listing of Claims:**

Claims 1-530 (Canceled).

531. (New) A method of treating an angiogenic disease or condition in an animal comprising administering to the animal an effective amount of a peptide having the formula:



wherein:

$P_1$  is:

Xaa<sub>1</sub> Xaa<sub>2</sub> His: or

Xaa<sub>1</sub> Xaa<sub>2</sub> His Xaa<sub>3</sub>;

$P_2$  is (Xaa<sub>4</sub>)<sub>n</sub>;

Xaa<sub>1</sub> is glycine, alanine, valine, leucine, isoleucine, serine, threonine, aspartic acid, asparagine, glutamic acid, glutamine, lysine, hydroxylysine, histidine, arginine, ornithine, phenylalanine, tyrosine, tryptophan, cysteine, methionine, or  $\alpha$ -hydroxymethylserine;

Xaa<sub>2</sub> is glycine, alanine,  $\beta$ -alanine, valine, leucine, isoleucine, serine, threonine, aspartic acid, asparagine, glutamic acid, glutamine, lysine, hydroxylysine, histidine, arginine, ornithine, phenylalanine, tyrosine, tryptophan, cysteine, methionine, or  $\alpha$ -hydroxymethylserine;

Xaa<sub>3</sub> is glycine, alanine, valine, lysine, arginine, ornithine, aspartic acid, glutamic acid, asparagine, glutamine or tryptophan;

Xaa<sub>4</sub> is any amino acid; and

n is 0-100;

or a physiologically-acceptable salt thereof.

532. (New) The method of Claim 531 wherein:

Xaa<sub>1</sub> is glycine, alanine, valine, leucine, isoleucine, serine, threonine, aspartic acid, glutamic acid, lysine, hydroxylysine, histidine, arginine, or  $\alpha$ -hydroxymethylserine, and

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Xaa<sub>2</sub> is glycine, alanine, valine, leucine, isoleucine, threonine, serine, asparagine, glutamine, cysteine, methionine, lysine, hydroxylysine, histidine, arginine, or  $\alpha$ -hydroxymethylserine.

533. (New) The method of Claim 531 wherein Xaa<sub>1</sub> is aspartic acid, glutamic acid, arginine, threonine or  $\alpha$ -hydroxymethylserine.

534. (New) The method of Claim 531 wherein Xaa<sub>2</sub> is glycine, alanine, valine, leucine, isoleucine, threonine, serine, asparagine, methionine, histidine or  $\alpha$ -hydroxymethylserine.

535. (New) The method of Claim 531 wherein Xaa<sub>3</sub> is lysine.

536. (New) The method of Claim 531 wherein:

Xaa<sub>1</sub> is aspartic acid, glutamic acid, arginine, lysine, threonine, serine or  $\alpha$ -hydroxymethylserine,

Xaa<sub>2</sub> is glycine, alanine, valine, leucine, isoleucine, threonine, serine, asparagine, methionine, histidine or  $\alpha$ -hydroxymethylserine, and

Xaa<sub>3</sub>, when present, is lysine.

537. (New) The method of Claim 536 wherein Xaa<sub>1</sub> is aspartic acid or glutamic acid and Xaa<sub>2</sub> is glycine, alanine, valine, leucine, isoleucine, threonine, serine or  $\alpha$ -hydroxymethylserine.

538. (New) The method of Claim 537 wherein Xaa<sub>2</sub> is glycine, alanine, valine, leucine or isoleucine.

539. (New) The method of Claim 538 wherein P<sub>1</sub> is Asp Ala His or Asp Ala His Lys.

540. (New) The method of Claim 539 wherein P<sub>1</sub> is Asp Ala His Lys.

541. (New) The method of Claim 536 wherein Xaa<sub>1</sub> is arginine, lysine, threonine, serine or  $\alpha$ -hydroxymethylserine, and Xaa<sub>2</sub> is glycine, alanine, valine, leucine, isoleucine, threonine, serine or  $\alpha$ -hydroxymethylserine.

542. (New) The method of Claim 541 wherein P<sub>1</sub> is Thr Leu His, HMS HMS His or Arg Thr His.

543. (New) The method of Claim 531 wherein n is 0-10.

544. (New) The method of Claim 543 wherein n is 0-5.

545. (New) The method of Claim 544 wherein n is 0.

546. (New) The method of Claim 531 wherein P<sub>2</sub> comprises a metal-binding sequence.

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547. (New) The method of Claim 546 wherein  $P_2$  comprises one of the following sequences:

(Xaa<sub>4</sub>)<sub>m</sub> Xaa<sub>3</sub> His Xaa<sub>2</sub> Xaa<sub>5</sub>,  
 (Xaa<sub>4</sub>)<sub>m</sub> His Xaa<sub>2</sub> Xaa<sub>5</sub>,  
 (Xaa<sub>4</sub>)<sub>m</sub> Xaa<sub>3</sub> Xaa<sub>2</sub> His Xaa<sub>3</sub>, or  
 (Xaa<sub>4</sub>)<sub>m</sub> Xaa<sub>3</sub> Xaa<sub>2</sub> His,

wherein Xaa<sub>5</sub> is an amino acid having a free side-chain -NH<sub>2</sub> and m is 0-5.

548. (New) The method of Claim 547 wherein Xaa<sub>5</sub> is Orn or Lys.

549. (New) The method of Claim 546 wherein  $P_2$  comprises one of the following sequences:

[(Xaa<sub>4</sub>)<sub>m</sub>Xaa<sub>3</sub>Xaa<sub>2</sub>HisXaa<sub>3</sub>]<sub>r</sub>,  
 [(Xaa<sub>4</sub>)<sub>m</sub>Xaa<sub>3</sub>Xaa<sub>2</sub>His]<sub>r</sub>,  
 [(Xaa<sub>4</sub>)<sub>m</sub>Xaa<sub>3</sub>Xaa<sub>2</sub>HisXaa<sub>3</sub>(Xaa<sub>4</sub>)<sub>m</sub>Xaa<sub>3</sub>Xaa<sub>2</sub>His]<sub>r</sub>, or  
 [(Xaa<sub>4</sub>)<sub>m</sub>Xaa<sub>3</sub>Xaa<sub>2</sub>His(Xaa<sub>4</sub>)<sub>m</sub>Xaa<sub>3</sub>Xaa<sub>2</sub>HisXaa<sub>3</sub>]<sub>r</sub>,

wherein Xaa<sub>5</sub> is an amino acid having a free side-chain -NH<sub>2</sub>, m is 0-5 and r is 2-100.

550. (New) The method of Claim 546 wherein  $P_2$  comprises a sequence which binds Cu(I).

551. (New) The method of Claim 550 wherein  $P_2$  comprises one of the following sequences:

Met Xaa<sub>4</sub> Met,  
 Met Xaa<sub>4</sub> Xaa<sub>4</sub> Met,  
 Cys Cys,  
 Cys Xaa<sub>4</sub> Cys,  
 Cys Xaa<sub>4</sub> Xaa<sub>4</sub> Cys,  
 Met Xaa<sub>4</sub> Cys Xaa<sub>4</sub> Xaa<sub>4</sub> Cys,  
 Gly Met Xaa<sub>4</sub> Cys Xaa<sub>4</sub> Xaa<sub>4</sub> Cys [SEQ ID NO:7],  
 Gly Met Thr Cys Xaa<sub>4</sub> Xaa<sub>4</sub> Cys [SEQ ID NO:8],  
 Gly Met Thr Cys Ala Asn Cys [SEQ ID NO:9], or  
 γ-Glu Cys Gly.

552. (New) The method of Claim 551 wherein  $P_2$  is Gly Met Thr Cys Ala Asn Cys [SEQ ID NO:9].

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553. (New) The method of Claim 531 wherein  $P_2$  comprises a sequence which enhances the ability of the peptide to penetrate cell membranes, reach target tissues, or both.

554. (New) The method of Claim 553 wherein  $P_2$  is hydrophobic or an arginine oligomer.

555. (New) The method of Claim 531 wherein at least one of the amino acids of  $P_1$  other than  $\beta$ -alanine, when present, is a D-amino acid.

556. (New) The method of Claim 556 wherein  $Xaa_1$  is a D-amino acid, His is a D-amino acid, or both  $Xaa_1$  and His are D-amino acids.

557. (New) The method of Claim 557 wherein all of the amino acids of  $P_1$  other than  $\beta$ -alanine, when present, are D-amino acids.

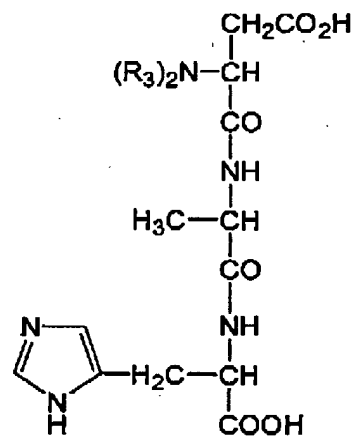
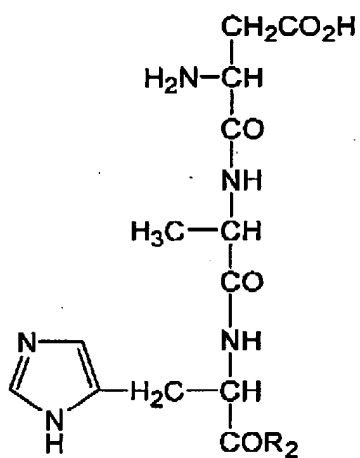
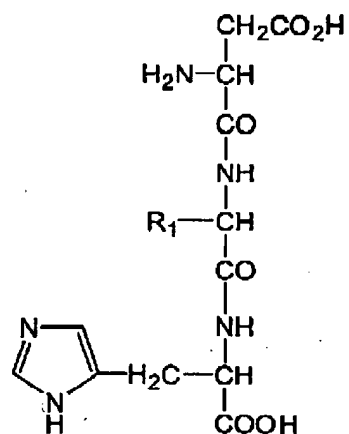
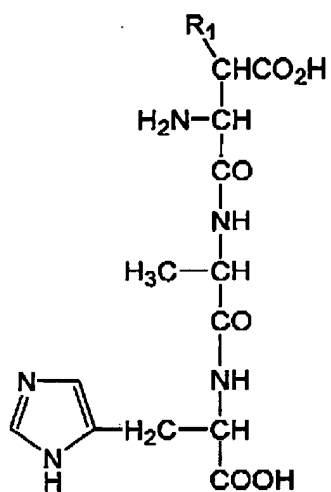
558. (New) The method of Claim 555 wherein at least 50% of the amino acids of  $P_2$  are D-amino acids.

559. (New) The method of Claim 531 wherein at least one amino acid of  $P_1$ , at least one amino acid of  $P_2$ , or at least one amino acid of  $P_1$  and at least one amino acid of  $P_2$  is substituted with (a) a substituent that increases the lipophilicity of the peptide without altering the ability of  $P_1$  to bind metal ions, (b) a substituent that protects the peptide from proteolytic enzymes without altering the ability of  $P_1$  to bind metal ions, or (c) a substituent which is a non-peptide, metal-binding functional group that improves the ability of the peptide to bind metal ions.

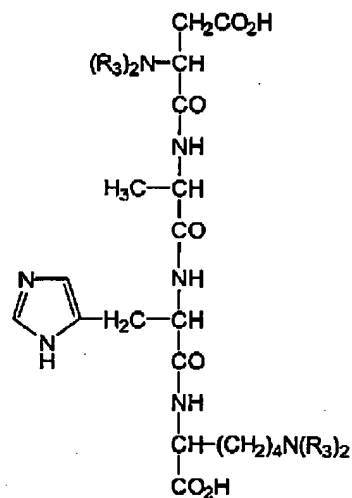
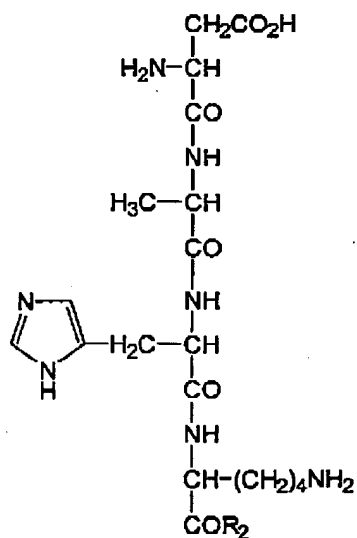
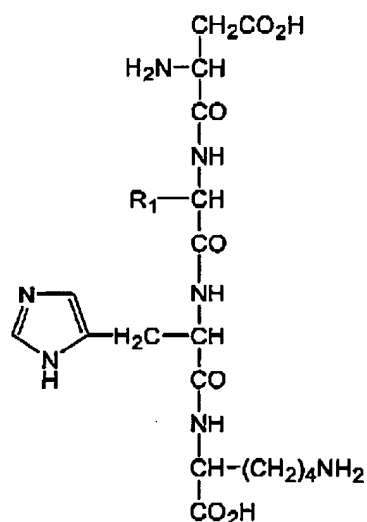
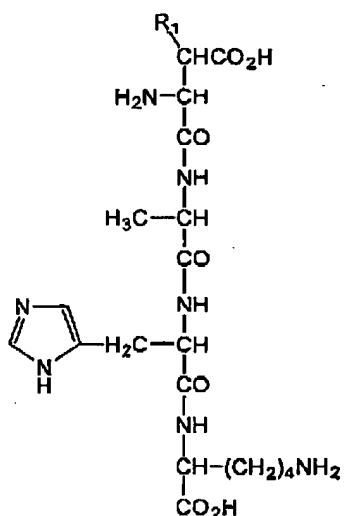
560. (New) The method of Claim 559 wherein the terminal  $-\text{COOH}$  of  $P_1$ - $P_2$  is substituted to produce  $-\text{COR}_2$ , wherein  $R_2$  is  $-\text{NH}_2$ ,  $-\text{NHR}_1$ ,  $-\text{N}(\text{R}_1)_2$ ,  $-\text{OR}_1$ , or  $-\text{R}_1$ , wherein  $R_1$  is an alkyl, aryl or heteroaryl.

561. (New) The method of Claim 559 wherein  $n$  is 0 and  $P_1$  has one of the following formulas:

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wherein:

 $R_1$  is an alkyl, aryl, or heteroaryl; $R_2$  is  $-NH_2$ ,  $-NHR_1$ ,  $-N(R_1)_2$ ,  $-OR_1$ , or  $-R_1$ ; and

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$R_3$  is H, a non-peptide, metal-binding functional group or the two  $R_3$  groups together form a non-peptide, metal-binding functional group.

562. (New) The method of Claim 561 wherein  $R_2$  is  $-NH_2$ .

563. (New) The method of Claim 531 wherein the method further comprises administering an effective amount of another metal-binding compound in combination with the peptide.

564. (New) The method of Claim 563 wherein the metal-binding compound binds iron.

565. (New) The method of Claim 564 wherein the iron-binding compound is deferoxamine mesylate.

566. (New) The method of Claim 563 wherein the metal-binding compound binds Cu(I).

567. (New) The method of Claim 566 wherein the Cu(I)-binding compound is a peptide.

568. (New) The method of Claim 567 wherein the Cu(I)-binding peptide comprises one of the following sequences:

Met Xaa<sub>4</sub> Met,

Met Xaa<sub>4</sub> Xaa<sub>4</sub> Met,

Cys Cys

Cys Xaa<sub>4</sub> Cys,

Cys Xaa<sub>4</sub> Xaa<sub>4</sub> Cys,

Met Xaa<sub>4</sub> Cys Xaa<sub>4</sub> Xaa<sub>4</sub> Cys,

Gly Met Xaa<sub>4</sub> Cys Xaa<sub>4</sub> Xaa<sub>4</sub> Cys [SEQ ID NO:7],

Gly Met Thr Cys Xaa<sub>4</sub> Xaa<sub>4</sub> Cys [SEQ ID NO:8],

Gly Met Thr Cys Ala Asn Cys [SEQ ID NO:9], or

$\gamma$ -Glu Cys Gly,

wherein Xaa<sub>4</sub> is any amino acid.

569. (New) The method of any one of Claims 531-568 wherein the angiogenic disease or condition is a neoplastic disease, a connective tissue disorder, psoriasis, an ocular angiogenic disease, a cardiovascular disease, a cerebral vascular disease, hemophiliac joints, an immune disorder, a benign tumor, hypertrophy, endometriosis, polyposis, or obesity.

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570. (New) The method of Claim 569 wherein the angiogenic disease or condition is a neoplastic disease.

571. (New) The method of Claim 570 wherein the neoplastic disease is a tumor.

572. (New) The method of Claim 571 wherein the tumor is located in the bladder, brain, breast, kidney, liver, pancreas, lung, cervix, ovary, prostate, stomach, intestines, colon, rectum, or uterus.

573. (New) The method of Claim 570 wherein the neoplastic disease is tumor metastasis.